Complete Summary

GUIDELINE TITLE

Clinical standards for the screening and management of acquired syphilis in HIV-positive adults.

BIBLIOGRAPHIC SOURCE(S)

Medical Society for the Study of Venereal Diseases (MSSVD). Clinical standards for the screening and management of acquired syphilis in HIV-positive adults. London (UK): Medical Society for the Study of Venereal Diseases (MSSVD); 2002 Feb 21. 9 p. [28 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Acquired syphilis
- Human immunodeficiency virus (HIV) infection

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Screening
Treatment

CLINICAL SPECIALTY

Emergency Medicine
Family Practice
Infectious Diseases

Internal Medicine
Preventive Medicine
Urology

INTENDED USERS

Health Care Providers
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

- To provide clinical standards for syphilis management in human immunodeficiency virus (HIV)-positive adults, including during outbreak situations
- To supplement and support the updated Clinical Effectiveness Group (CEG) guidelines and Public Health Laboratory Service (PHLS) sexually transmitted infection outbreak guidelines by describing minimum clinical standards

TARGET POPULATION

HIV-positive adults in the United Kingdom who are at risk of sexually transmitted infection, specifically, syphilis

INTERVENTIONS AND PRACTICES CONSIDERED

Screening

1. Sexual risk assessment
2. Screening for sexually transmitted infections
3. Syphilis serology consisting of enzyme immunoassay (EIA) or Treponema pallidum haemagglutination (TPHA), or equivalent, combined with a reagin test, usually the Venereal Disease Research Laboratory (VDRL) or rapid plasma reagin (RPR)

Diagnosis

1. Physical examination including oral examination, assessment for clinical features of syphilis in HIV-positive individuals, and cardiovascular exam including pulse and blood pressure
2. Laboratory testing
    - Fluorescent treponemal antibody absorption test (FTA-abs)
    - Dark ground microscopy
    - Direct fluorescent antibody (DFA) test
    - Polymerase chain reaction (PCR)
    - Pregnancy test
3. Neurological examination and, if symptomatic:
    - Head scan
    - Lumbar puncture

Treatment

1. First line regimen: Intramuscular penicillin G, plus oral probenecid OR reconstituted Jenacillin A
2. Second line regimens
    - Oral doxycycline
    - Oral amoxycillin with probenecid
    - Ceftriaxone

Management

1. Partner notification
    - Provider referral as needed
2. Follow-up
    - Reagin titre at scheduled intervals

MAJOR OUTCOMES CONSIDERED

- Sensitivity, specificity and positive predictive value of diagnostic tests for sexually transmitted diseases in HIV-infected individuals
- Rate of syphilis infection in HIV-infected individuals
- Rate of treatment failure including incidence of clinical or serological relapse

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Searches of MEDLINE, Cochrane, Embase, and scientific abstract data were performed.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Testing for Syphilis in Human Immunodeficiency Virus (HIV)-Positive Individuals

MINIMUM STANDARD: All HIV care providers must offer sexual risk assessment and, if appropriate, screening for sexually transmitted infections every 6 months for HIV-positive patients under follow-up. This may be within the clinic itself or by referral to appropriate colleagues.

A sexual history should be obtained and documented at least every 6 months in those being followed up for HIV. It is essential that HIV service providers consider sexual health as an integral component of routine HIV care. Obstacles that may prevent this are lack of training or discomfort of clinic staff, insufficient facilities or lack of time during consultations (Butt & Nandwani, 2001). Where HIV care is provided in non-genitourinary medicine (GUM) settings, formalised links or care pathways should be established to ensure that adequate sexual health care is integrated into patient management.

Syphilis Screening as Part of Ongoing HIV Clinical Care

MINIMUM STANDARD: All HIV-positive patients under regular follow-up should have syphilis serology documented at baseline and subsequently and 12 monthly thereafter.

Evidence for the optimal screening interval is lacking at present and therefore this recommendation is based on expert opinion and current practice. Refer to the original guideline document for the rationale.

It is recognised that a history of sexual activity may not be elicited from all HIV-positive individuals under follow-up, however the recommendation for annual serological testing is made on the basis that a full sexual history taking may not be available in the HIV clinic setting and that treponemal infection can relapse without new exposure. If a patient declines annual syphilis serology, this should be documented, with the reason, in the casenotes.

Screening can be performed in a routine situation using the syphilis enzyme immunoassay (EIA) or the treponema pallidum haemagglutination (TPHA) or equivalent combined with a reagin test, usually the Venereal Disease Research Laboratory (VDRL) or rapid plasma reagin (RPR). Tests must be performed in laboratories with appropriate quality accreditation.

Syphilis Screening in an Outbreak Situation

MINIMUM STANDARD: In an outbreak situation, serological testing for syphilis should be offered to HIV-positive individuals every 3 months, to coincide with HIV follow-up attendances.

Since many of the United Kingdom (UK) outbreaks have been characterised by both the high number of anonymous contacts and the high rate of associated HIV infection, it is recommended that the HIV positive population should be considered for more frequent screening even where no contact with a case of known syphilis is reported. This recommendation is based on expert opinion rather than evidence and should be reviewed in the light of emerging information as the current epidemiology in the United Kingdom (UK) unfolds (refer to section 2.2 of original guideline for details on outbreak characteristics).

Clinical Features of Syphilis in HIV-positive Individuals

Genital ulceration in primary syphilis can present as atypical and/or multiple ulcers, and may resemble an episode of genital herpes. Features of syphilis can easily be mistaken for clinical manifestations of HIV infection. Several cases of syphilis in the United Kingdom (UK) outbreaks have been transmitted by oro-genital sexual contact alone, therefore careful oral examination with an appropriate light source is recommended.

Features of syphilis in HIV include:

- Generalized lymphadenopathy
- Splenomegaly
- Hepatitis
- Skin rashes and/or alopecia
- Oral manifestations
- Cognitive impairment
- Meningitis
- Cranial nerve palsies

- Myelopathies
- Uveitis (commoner in HIV-positives) (Becerra et al., 1989)

Although open to debate, there appears to be a significant risk of neurological involvement in early syphilis in patients who are HIV-positive (Johns, Tierney, & Felsenstein, 1987; Berger, 1991; Bordon et al., 1995), and so it appears plausible that neurological symptoms may be more likely in the context of HIV. Therefore a high index of suspicion backed by serological testing is required to exclude syphilis.

Diagnosis of Syphilis in HIV-positive Individuals

Where lesions that are clinically suspicious of primary syphilis are identified, attempts must be made to identify treponemes by dark ground microscopy. Where HIV care is provided in a non-GUM setting, referral to an appropriate clinic to enable this is required. Treponema pallidum can also be demonstrated using a direct fluorescent antibody (DFA) test or by polymerase chain reaction (PCR) where available. These latter two methods may help distinguish T. pallidum from commensal treponemes in oral lesions.

Following a positive syphilis screen (enzyme immunoassay or treponemal plus regain tests), all positive results should be confirmed on a second sample with supplementary tests. The Fluorescent Treponemal Antibody absorption test (FTA-abs) should be performed if early syphilis is suspected. In HIV patients, consideration should be given to a possible prozone phenomenon (especially in cerebrospinal fluid) producing a false negative result and dilutions performed.

Where serology is equivocal, this should be repeated and further management based upon the level of clinical suspicion. Re-infection or relapse of syphilis should be considered where the reagin titre increases 4-fold.

In patients where there is a history of previously treated syphilis, serology is likely to remain positive lifelong. In such situations, strenuous efforts should be made to confirm that the treatment regimen was complete and effective (Clinical Effectiveness Group, 1999), particularly if the individual is suspected or known to have been HIV positive at the time of syphilis treatment (see treatment recommendations below).

If the individual is found to have received suboptimal therapy then re-treatment should be considered, particularly in the presence of clinical features that could be consistent with syphilis.

It is also recommended that a pregnancy test should be performed after appropriate discussion in all HIV-positive women found to be infected with syphilis.

Treatment of Syphilis in HIV-positive Individuals

Treatment Regimens

MINIMUM STANDARD: Treatment of syphilis in HIV-positive individuals should be sufficient to produce treponemicidal levels in both serum and the cerebral spinal fluid (CSF) to prevent future neurosyphilis. (refer to the National Guideline Clearinghouse [NGC] summary of the Medical Society for the Study of Venereal Diseases [MSSVD] Clinical Effectiveness Group [CEG] guidelines 2002 national guidelines on the management of early syphilis, and 2002 national guidelines for the management of late syphilis).

Penicillin remains the treatment of choice. A commonly used regimen in the United Kingdom (UK) is intramuscular Procaine penicillin G plus oral probenecid or reconstituted Jenacillin A (refer to section 5.1 in original guideline document for details). Although this involves the administration of large volumes over an extended time period, it remains the recommended first-line therapy and strenuous efforts should be made to use this regimen wherever possible. Appropriate local systems should be established to ensure that injections can be given when clinics are shut (e.g., utilising inpatient HIV units, accident and emergency departments or other appropriate arrangements).

By treating all stages of syphilis in HIV adequately with a CSF treponemicidal regimen, future confusion about sub-optimal therapy is avoided should the patient develop neurological or psychiatric symptoms and/or signs.

Second line regimens include oral doxycycline or oral amoxycillin with probenecid, but these are considered sub-optimal in HIV as they are not known to be fully treponemicidal in the CSF.

Ceftriaxone has been used as an alternative agent with reported good CSF penetration, but data is currently limited. There is also insufficient data to support the use of azithromycin at present. Erythromycin is not recommended because of poor CSF penetration.

Need for Lumbar Puncture

MINIMUM STANDARD: All HIV-infected patients with positive syphilis serology must have a full documented neurological examination.

If neurological symptoms or signs are present, a head scan and lumbar puncture is required to exclude other HIV related conditions. Asymptomatic HIV positive patients do not require a lumbar puncture unless they are going to be treated with a course of antibiotics where there is uncertainty about whether CSF treponemicidal levels will be achieved. Procaine penicillin is known to be treponemicidal in CSF using the regimen above.

The interpretation of CSF syphilis tests in HIV-positive individuals can be difficult even in the absence of blood contamination. Ideally, the first CSF sample should not be sent for syphilis tests owing to the risk of blood contamination.

- Mononuclear pleocytosis and elevated protein can occur in HIV without neurosyphilis (Berger, 1991).
- The CSF reagin test is insensitive in HIV (Davis & Schmitt, 1989).

- A negative CSF fluorescent treponemal antibody absorption test (FTA-abs) or micro hemagglutination treponemal (MHA-TP) probably excludes neurosyphilis (Davis & Schmitt, 1989; Simon, 1985)

It also good practice to document a full physical examination including cardiovascular examination with pulse and blood pressure readings. Further investigations such as a chest radiograph and an electrocardiogram are not routinely required in HIV-positive individuals with early syphilis. These are often performed in later disease, but the evidence for this practice is lacking.

Tests for Other Sexually Transmitted Infections

MINIMUM STANDARD: A full sexual health screen (including investigations for gonorrhoea and chlamydia) should be performed in all patients with proven or suspected syphilis.

Where HIV care is provided in a non-GUM setting, appropriate referral should be made at the earliest opportunity. Samples may be required from multiple anatomical sites to exclude co-infection.

Partner Notification

Where sexual partners are traceable, strenuous attempts should be made to recommend screening of such contacts for syphilis (and other sexually transmitted infections including HIV). Provider referral should be offered as an alternative means of partner notification. If HIV care is provided in a non-GUM setting, involvement of health advisers in local genitourinary medicine services (where such procedures are routine) is recommended.

Where sexual partners are untraceable, consideration of alternative strategies for screening and outbreak control should be considered (Public Health Laboratory Service, 2001; CDR Weekly, 2000).

Follow-up

Unless there are circumstances to suggest inadequate response to initial therapy, all patients should be monitored for evidence of clinical or serological relapse at 3 monthly intervals to one year and then at least annually lifelong.

Follow-up should include the reagin titre. Relapse or reinfection should be considered if there is a 4-fold rise in the Venereal Disease Research Laboratory (VDRL) or rapid plasma reagin (RPR) titre.

Management of Individuals at High Risk but Unknown HIV Status

Where an individual is unwilling or unable to have an HIV antibody test performed, but HIV is considered likely on clinical grounds, it is recommended that treatment should be administered as per individuals with proven HIV infection.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation. Recommendations based on expert opinion and/or clinical practice rather than evidence are identified in the original guideline document.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Improved screening and management of syphilis in HIV-positive individuals
- Decreased rates of syphilis infection
- Improved accuracy of diagnostic testing for syphilis in HIV-positive individuals
- By treating all stages of syphilis in HIV adequately with a cerebral spinal fluid (CSF) treponemicidal regimen, future confusion about sub-optimal therapy is avoided should the patient develop neurological or psychiatric symptoms and/or signs.

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Given the recent syphilis outbreaks, the MSSVD HIV Special Interest Group was asked to propose clinical standards for syphilis management in HIV-positive adults including during outbreak situations as part of a larger piece of work looking at the sexual health of HIV-positive individuals. This clinical guideline supplements the updated Clinical Effectiveness Group (CEG) guidelines and Public Health Laboratory Service (PHLS) sexually transmitted infection outbreak guidelines and is intended to support rather than replace the guidance contained in these documents, by describing minimum standards and making these available to all those involved in HIV care.
- Serologic testing must be performed in laboratories with appropriate quality accreditation.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Audit against the standards (for testing, screening, and treatment) as stated in the guideline to determine implementation effectiveness.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Medical Society for the Study of Venereal Diseases (MSSVD). Clinical standards for the screening and management of acquired syphilis in HIV-positive adults. London (UK): Medical Society for the Study of Venereal Diseases (MSSVD); 2002 Feb 21. 9 p. [28 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002 Feb

GUIDELINE DEVELOPER(S)

British Association of Sexual Health and HIV - Medical Specialty Society

SOURCE(S) OF FUNDING

Medical Society for the Study of Venereal Diseases

GUIDELINE COMMITTEE

MSSVD HIV Special Interest Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors: R. Nandwani, M. Fisher

HIV Special Interest Group: M. Fisher (Chair); R. Nandwani; M. Nelson, B. Peters, K. Radcliffe, I. Williams

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

ENDORSER(S)

Medical Foundation for AIDS and Sexual Health (UK) - Private Nonprofit Organization

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Medical Society for the Study of Venereal Diseases (MSSVD) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Summary of clinical standards for acquired syphilis in HIV-positive adults. London (UK): Medical Society for the Study of Venereal Diseases (MSSVD); 2002 Feb 21. 2 p.

Electronic copies: Available in Portable Document Format (PDF) from the Medical Society for the Study of Venereal Diseases (MSSVD) Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on January 8, 2003. The information was verified by the guideline developer on January 24, 2003.

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